

## **REMARKS**

### **Status of the claims**

Claims 31, 33, 35-39 and 45 to 46 are in the case.

Claims 32, 34 and 44 have been cancelled and claims 45 and 46 are newly added.

Claims 31, 33, 35, 38, 39 and 44 have been amended in view of the Office Action and to better define what the Applicants consider their invention, as fully supported by an enabling disclosure. Additional support for the amendments to the claims can be found in the original claims.

Reconsideration in view of the following remarks and entry of the foregoing amendments are respectfully requested.

### **Election/restriction requirement**

Applicants have removed the non-elected species from claims 31, 38 and 39 and withdrawn claims 1, 9, 11-15, 17-24, 26-30 and 41-43.

### **Information Disclosure Statement:**

Applicants enclose a copy of the Bhardwaj *et al.* reference which was missing from the Information Disclosure Statement filed 17 August 2005.

### **Claim objections**

Claim 39 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim.

Claim 31 has been amended to become an independent claim. Accordingly, claim 39 is no longer depending on another multiple dependent claim. Withdrawal of the objection is respectfully requested.

Claims 31-38 and 44 are objected to as depending from a withdrawn claim.

Claim 44 was cancelled. The features of withdrawn claim 1 have been incorporated into claim 31 and reference to claim 15 has been removed following the restriction requirement. Accordingly, claim 31 is now an independent claim. Withdrawal of the objection is respectfully requested.

### **Claim Rejections:**

#### **35 USC §112, 2<sup>nd</sup> paragraph**

Claims 32-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Claim 31 (and therefore dependent claims 32-38) is considered indefinite because the Patent Office finds unclear whether the phrase "for a time sufficient to allow expansion of said stem cells" refers only to "an effective amount of a composition as defined in claim 15" or whether it also is meant to limit the phrase "an effective amount of a factor as defined in claim 1".

In view of the restriction requirement, Applicants have removed the reference to the composition of claim 15 and the phrase "for a time sufficient to allow expansion of said stem cells" has been moved in the beginning of the claim to further clarify the claim.

Claim 32 is also rejected as lacking antecedent basis because it is indirectly dependent from a withdrawn claim. In view of the amendments to claim 31, which now incorporates the language of claim 1, Applicants believe that the objection is no longer applicable.

Claim 33 is also rejected as being indefinite because the phrase "further comprising a step of treating said stem cell a HOX peptide encoded by a HOX nucleotide sequence" appears to be missing a word between "cell" and "a". The term "with" was added

accordingly.

Finally claims 34-35 and dependent claim 36 are rejected as lacking antecedent basis for reciting the limitation "said amino acid sequence". Claim 34 was cancelled. Claim 35 was amended accordingly.

In view of the foregoing, Applicants respectfully request that the rejections under 35 USC 112, 2<sup>nd</sup> paragraph be withdrawn.

### **35 USC §112, 1<sup>st</sup> paragraph**

Claims 31-38 and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

According to the Patent Office, "the stem cell expansion factors are defined by the claims as comprising an amino acid sequence having the expansion enhancement activity of a peptide encoded by a Hox nucleotide sequence enhancing expansion of a stem cell population, and wherein the factor is able to cross a cell membrane. The rejected claims thus comprise a genus of proteins that are defined by function: (1) have the enhancement activity of a hox peptide, and (2) are capable of crossing the cell membrane", which is not considered as being supported by the disclosure.

The language cited by the Examiner is that found in claim 15. However, the response to the restriction requirement withdrew claim 15. Claim 31 was amended to cancel reference to claim 15 and to incorporate the subject matter of claim 1. Furthermore, in order to advance the prosecution of the instant application, it is now specified in claim 31, 33 and 35 that the recited HOX is HOXB4. Withdrawal of the objection is respectfully requested.

### 35 USC §102(a)

Claims 31-38 and 44 are rejected by the Patent Office under 35 U.S.C. 102(a) as being anticipated by Buske *et al.* in "Deregulated expression of HOXB4 enhances the primitive growth activity of human hematopoietic cells" (Blood, 1 August 2002, Vol. 100, No:3, pp. 862-868).

According to the Patent Office, "Claims 31 and 32 read on a method comprising: treating stem cells with an effective amount of a factor comprising a blocker which reduces expression level of at least one gene normally limiting HOX-induced expansion of stem cells, whereby reducing expression level of said gene enhances expansion of stem cells containing a HOX/HOXB4 peptide".

The Applicants traverse as follows:

The Examiner states that "Buske et al. teach treating said stem cell with a HOX peptide encoded by a HOX nucleotide sequence. Buske et al teach a blocker which reduces expression level of at least one gene normally limiting HOX-induced expansion of stem cells, whereby reducing expression level of said gene enhances expansion of stem cells containing a HOX peptide (e.g. abstract and Figure 1 and legend).

Buske *et al.*'s abstract, Figure 1 and Figure 1 legend referred to by the Examiner describe or show the overexpression of HOXB4 induced by retroviral gene transfer in primitive human cord blood cells. It does not show the use of a factor which comprises a blocker for reducing the expression of a PBX gene.

Buske *et al.* thus does not teach the claimed method for enhancing expansion of stem cells which comprises treating stem cells with an effective amount of a stem cell expansion factor comprising a blocker which reduces the expression level of at least one PBX gene, whereby reducing the expression level of said PBX gene enhances expansion of stem cells containing a HOXB4 peptide.

In view of the above and of the amendments to the claims, Applicants respectfully request that the objection under 35 USC 102(b) be withdrawn.

### **35 USC §103(a)**

Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Largman *et al.* (US Patent No. 5,837,507) and in view of Frankel *et al.* (US Patent No. 5,804,604).

The Applicants traverse as follows:

Claims 35 and 36 ultimately depend from claim 31. Hence claims 35 and 36 contain all the limitations of claim 31 (as well as claim 33). Claim 31 concerns a method for enhancing expansion of stem cells, which comprises treating stem cells with an effective amount of a stem cell expansion factor comprising a blocker which reduces the expression level of at least one PBX gene, whereby reducing the expression level of said PBX gene enhances expansion of stem cells containing a HOXB4 peptide.

None of the prior art cited by the Patent Office, taken alone or in combination, teaches or suggests blocking the expression level of at least one PBX gene to enhance expansion of stem cells containing a HOXB4 peptide. Applicants submit that the claims are inventive over Largman, Frankel, and/or Buske *et al.* Reconsideration and withdrawal of the objection is respectfully requested.

### **Double Patenting**

Claims 31-38 and 44 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7, 9, 12 and 13 of copending Application No. 10/727,580 (herein "the '580 application").

The Patent Office states that “[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because amended claims 31-38 and 44 are now generic to or essentially identical to all that is recited in the presently amended copending claims 7, 9, 12 and 13 of the '580 application. In other words, the Patent Office considers claims 31-38 and 44 anticipated by claims 7, 9, 12 and 13 of the '580 application. The claims of the '580 application are narrower in scope than the instant claims in that they require the limitations of the instant dependent claims in the copending base claim.”

Claims 32, 34 and 44 are cancelled. Claims 31, 33, 35-38 now recite a method for enhancing expansion of stem cells, which comprises treating stem cells with an effective amount of a stem cell expansion factor comprising a blocker which reduces the expression level of at least one PBX gene, whereby reducing the expression level of said PBX gene enhances expansion of stem cells containing a HOXB4 peptide. These claims are thus not anticipated by claims 7, 9, 12 and 13 of the '580 application which do not disclose or suggest a blocker which reduces the expression level of at least one PBX gene. Reconsideration and withdrawal of the objection is respectfully requested.

#### Concluding Remarks

In view of the above amendment and remarks, Applicants believe that the pending application is in condition for allowance. Should there be any issues requiring discussion in this application, the Examiner is invited to contact Julie Gauvreau, Registration No. 52,532, at (514) 397-4374.